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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: :  
Giorgio BERTOLINI et al. : Attorney Docket: 2003IT304  
Serial No.: to be Assigned :  
Filed: April 21, 2006 :  
Title: PROCESS FOR THE PREPARATION OF DOXIFLURIDINE

Transmittal Letter  
Notification of Amendments Under PCT Article 34

Mail Stop:  
Commissioner for Patents  
P. O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Preliminary to the examination of the above-identified application, an Amendment was filed under Article 34 of the Patent Cooperation Treaty prior to the International Preliminary Examination. Please note that the attached pages, 8 and 9, Claims 1-8, were filed with the European Patent Office.

Applicant respectfully requests submission of this page before examination of the application and before entry of the Preliminary Amendment.

Respectfully submitted,

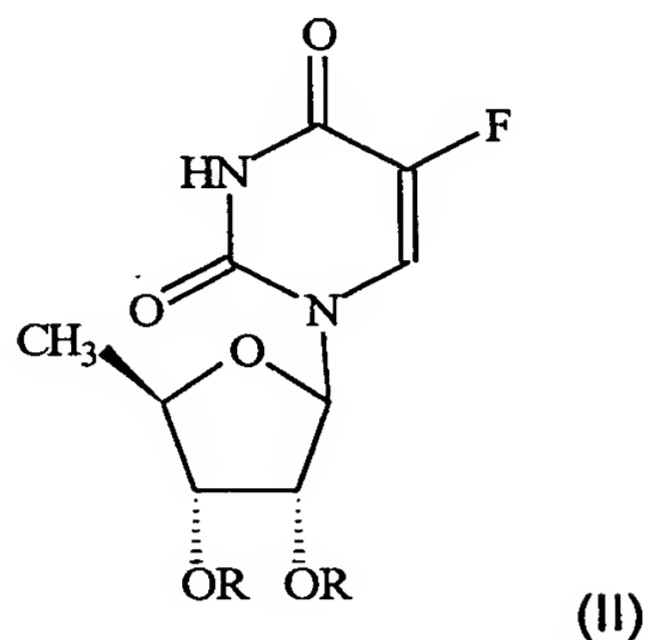
  
Richard P. Silverman, Reg. No. 36,277

**(CUSTOMER NUMBER 25,255)**  
Clariant Corporation  
Industrial Property Department  
4000 Monroe Road  
Charlotte, North Carolina 28205  
Direct Dial: 704/331-7156  
Facsimile: 704/331-7707

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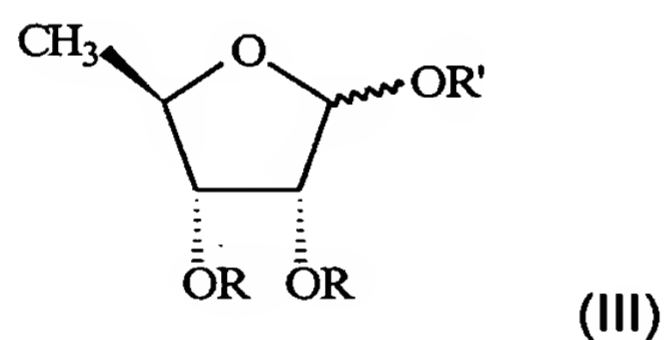
**CLAIMS**

1. A process for preparing a compound of formula



in which R represents linear or branched C<sub>1</sub>-C<sub>5</sub> aliphatic acyl or benzoyl, optionally substituted with C<sub>1</sub>-C<sub>5</sub> alkyls, C<sub>1</sub>-C<sub>5</sub> alkoxyis or halogens,

- 10 which comprises the reaction of coupling of a compound of formula

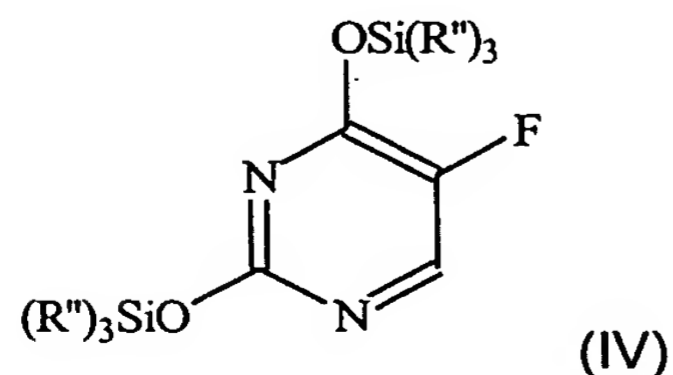


in which

- 15 R represents a linear or branched C<sub>1</sub>-C<sub>5</sub> aliphatic acyl or benzoyl, optionally substituted with C<sub>1</sub>-C<sub>5</sub> alkyls, C<sub>1</sub>-C<sub>5</sub> alkoxyis or halogens,  
R' represents R or a linear or branched C<sub>1</sub>-C<sub>5</sub> alkyl,

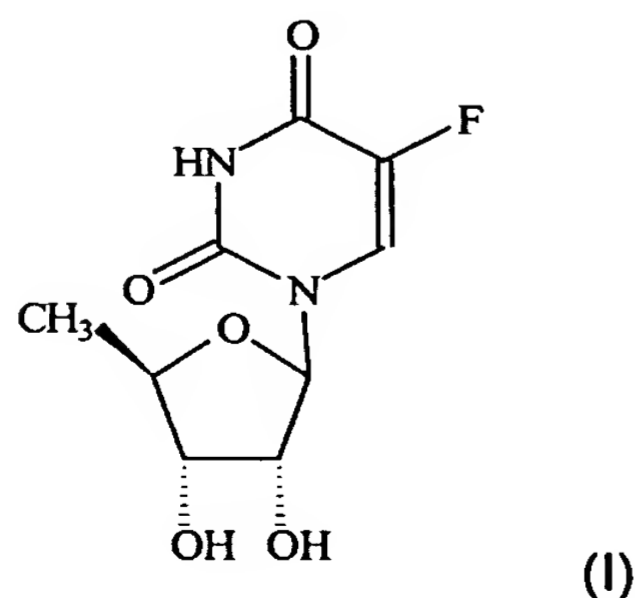
with a compound of formula

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in which R", being identical or different, represents a C<sub>1</sub>-C<sub>6</sub> alkyl or a phenyl, in the presence of a Lewis acid and in an inert organic solvent, characterized in that said Lewis acid is added at a temperature below -10°C.

- 5      2.      A process according to claim 1 in which said addition of catalyst is carried out at a temperature between approx. -15 and -20°C.
3.      A process according to claim 1 in which, on completion of said addition of catalyst, the reaction mixture is held further at the same temperature.
- 10      4.      A process according to claim 1 in which R and R' represent acyl, preferably acetyl, and R" represents methyl.
- 15      5.      A process according to claim 1 in which said Lewis acid is selected from trimethylsilyltrifluoromethanesulphonate and tin tetrachloride, and is preferably tin tetrachloride.
6.      A process according to claim 1 in which said inert organic solvent is selected from chlorinated solvents or aromatic solvents, preferably chlorinated solvents.
- 20      7.      A process according to claim 1 in which said compound of formula II, in which R has the meanings stated above, is further submitted to a reaction of deprotection to give doxifluridine of formula I.
- 25      8.      A process for the preparation of doxifluridine of formula



that comprises a process according to one of the claims from 1 to 7.